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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,813	01/29/2004	Puwen Zhang	AHPWA1DUSA	5696

38199 7590 09/20/2007  
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EXAMINER
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BETTON, TIMOTHY E

ART UNIT	PAPER NUMBER
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1614

MAIL DATE	DELIVERY MODE
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09/20/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No. 10/767,813	Applicant(s) ZHANG ET AL.	
	Examiner Timothy E. Betton	Art Unit 1614	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 August 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 49-51 is/are pending in the application.
- 4a) Of the above claim(s) 51 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 49-50 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>See Continuation Sheet</u>                                    | 6) <input type="checkbox"/> Other: _____                          |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :11/04/2004 and 30 April 2004, 16 sheets .

## **DETAILED ACTION**

### ***Election of Species***

Applicant's election in the reply filed on 2 August 2007 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants' hereby elect the invention of Group II, i.e., a compound. Claims 49-50 read on this election. Likewise, in response to the requirement to elect one specific compound from claim 49, Applicants hereby elect [3-(4,4-dimethyl-2-oxo- 1,4-dihydro-2H-3, 1-benzoxazin-6-yl)-5- fluorophenyl] acetonitrile. Claims 49 and 50 read on this election.

### ***Status of the Claim***

Claims 1-48 are cancelled. Claim 49 has been amended.

Claims 50 and 51 are new. However, claim 51 is withdrawn from examination due to being directed to a non-elected set of compounds. Instant claims 49 –50 are under examination.

### ***Claim Rejection-35 U.S.C. §112, 1st paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 49-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant specification discloses in Example 133 (p. 101), a synthesis or a synthetic methodology of 3-(4,4-Dimethyl-2-oxo-1,4-dihydro-2H-benzold) [1-3]-oxazin-6-yl)-5-fluorophenylacetonitrile as follows:

To a solution of 3-bromo-5-fluorobenzaldehyde(22.25g, 0.11 mole) in methanol at rt was added NaBH<sub>4</sub>(2.07g, 0.055 mole) stirred at rt for 2 hr. The reaction was quenched with H<sub>2</sub>O, and concentrated. The residue was diluted with diethyl ether, washed with 1 N HCl, brine, dried over MgSO<sub>4</sub>, and concentrated. 3-Bromo-5-fluorobenzyl alcohol was obtained as a colorless oil was collected (14.6 g, 65%). <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 8 4.50 (m, 2H), 5.44(t, 3H, J= 5.93 Hz), 7.16 (dd, 1H, J = 1.09, 8.79 Hz), 7.36 (s, 1H), 7.38 (dd, 1H, J = 2.99, 6.15 Hz); Anal. Calc. For 25 C<sub>7</sub>H<sub>6</sub>Br<sub>2</sub>FO: C, 41.01, H, 2.95. Found: C, 41.30, H, 3.01.

To a solution of 3-Bromo-5-fluorobenzyl alcohol (2.3g, 0.011 mole) in CH<sub>2</sub>Cl<sub>2</sub> (15mL) was added 12.4 mL of 1.0M PBr<sub>3</sub> (3.33g, 0.0123 mole) in CH<sub>2</sub>Cl<sub>2</sub>, stirred for 3 hr, diluted with ether (100mL), washed with H<sub>2</sub>O (50ml,3X), dried over MgSO<sub>4</sub>, concentrated, and purified by column chromatography using 1:9 ethyl 30 acetate/hexane as an eluant solvent system 3-Bromo-5-fluorobenzyl bromide was obtained as a white crystalline material was obtained, mp 41-43°C. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 6 4.69 (s, 2H), 7.52 (d, 1H, J = 1.76 Hz) 7.54 (d, 1H, J = 1.91 Hz), 7.56 (s, 1H); MS(EI): M<sup>+</sup>. m/z 266 ; Anal. Calc. For C<sub>7</sub>H<sub>5</sub>Br<sub>2</sub>F: C, 31.38, H, 1.88. Found: C, 31.75, H, 1.78.

To a solution of 3-bromo-5-fluorobenzyl bromide (3.2g, 0.0112 mole) in 1,4-dioxane (20mL) was added a solution of KCN (0.82g, 0.013 mole) in H<sub>2</sub>O (5mL) and EtOH (5mL), refluxed for 2 hours, extracted with ether, washed with brine, dried over MgSO<sub>4</sub>, and concentrated. Column chromatography was performed using hexane/ethyl acetate (19:1). 3-Bromo-5-fluorophenylacetonitrile was obtained as a colorless oil: <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 6 4.15 (s, 2H), 7.29 (d, 1H, J= 9.37 Hz), 7.47 (s, 1H), 7.55 (d, 1H, J = 8.45 Hz); MS(EI) M<sup>+</sup> m/z 213 ; Anal. Calc. For C<sub>8</sub>H<sub>5</sub>BrFN: C, 44.89, H, 2.35, N, 6.54. Found: C, 44.88, H, 2.32, N, 6.46.

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The title compound was prepared according to the procedure B from 3-bromo-5-fluorophenylacetonitrile and (1,4-dihydro-4, 4-dimethyl-2-oxo-2H-3, 1-benzoxazin-15(6H)-yl) boronic acid. A white solid was obtained and recrystallized from ethanol/ether: mp 218-220. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) δ 1.67 (s, 6H), 4.11 (s, 2H), 6.98 (d, 1H, J = 8.92 Hz), 7.18 (d, 1H, J = 9.26 Hz), 7.52-7.62 (m, 3H), 10.37 (s, 1H); MS(EI) (M-H)<sup>+</sup> m/z 309; Anal. Calcd. For C<sub>15</sub>H<sub>15</sub>FN<sub>2</sub>O<sub>2</sub>: C, 69.67, H, 4.87, N, 9.03. Found: C, 69.78, H, 4.97, N, 8.36.

However, the last paragraph of the synthetic methodology fails to adequately disclose how to make the claimed title compound. Granted, the title compound is cited to have been prepared according to procedure B, but there is no definitive explanation of what occurs during procedure B or at least a complete and definitive representation of method steps directed to enabling claimed invention. Also, there is no elucidation in regard to an adequate manner of making the claimed compound from the disclosure cited under Example 133. Instant specification cites that a white solid is obtained but the same specification is absent of any adequate preparation steps and/or explanation directed to making the compound as claimed.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include:

- 1) the quantity of experimentation necessary
- 2) the amount of direction or guidance provided
- 3) the presence or absence of working examples
- 4) the nature of the invention

- 5) the state of the art
- 6) the relative skill of those in the art
- 7) the predictability of the art and
- 8) the breadth of the claims

***The nature of the art***

The nature of the art is drawn to cyclocarbamate derivatives as progesterone receptor modulators.

***The quantity of experimentation necessary,***

***The amount of direction or guidance provided/presence or absence of  
working examples and predictability***

The teachings of Example 133 in instant specification does not adequately disclose how to make the claimed compound. The skilled artisan would not instantly be apprised of the process, which encompasses procedure B from the disclosure of Example 133. It cannot be determined from the disclosure as mentioned to what quantitative degree procedure B yields in the process of preparation via any experimentation, explanation, and/or description.

The title compounds is cited to have been prepared but there is no direction or guidance, which supports a concise and clear process for making 3-(4,4-Dimethyl-2-oxo-1,4-dihydro-2H-benzod[1,3]-oxazin-6-yl)-5-fluoro-phenylacetonitrile.

In instant specification, the disclosure of Example 133 cite solutions consisting of 3-bromo-5 fluorobenzaldehyde, 3-bromo-5-fluorobenzyl bromide, 3-Bromo-5-

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fluorophenylacetonitrile, etc. However, The last paragraph cites (1,4-dihydro-4, 4-dimethyl-2-oxo-2H-3, 1-benzoxazin-15 6-yl) boronic acid in the making of the claimed compound, but yields no prior explanation as to why it would initially be synthesized with the 3-bromo-5-fluoroacetonitrile in order to make claimed compound. It is unclear as to what would be exactly entailed in the preparation of the title compound/ claimed compound of instant claims.

Also, the quantity of experimentation cannot be accurately determined in view of an unclear synthetic methodology directed to making the claimed compound. The process according to Example 133 does not flow in such a way as to convey to the skilled artisan that the specification is enabling with respect to how to make the claimed compound.

The skilled artisan recognizes the necessity of clear and concise synthetic methodologies in order to properly assess enablement. Otherwise, unpredictability is high due to the absence of any adequate and complete representation in reference as to how to make the claimed compound.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone



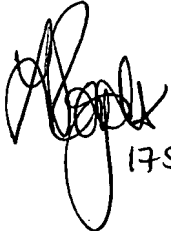
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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

 9/17/07  
ARDIN H. MARSCHEL  
SUPERVISORY PATENT EXAMINER

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